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ARTICLE

Efficacy of a Quail Eggs-Based Dietary Supplement for Allergic Rhinitis: Results of a Single-Arm Trial

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ABSTRACT

Previous data suggested the potential treatment effect of a proprietary quail eggs-based blend on allergic rhinitis (AR) symptoms, induced by allergen challenge. We herein aimed to investigate the efficacy and safety of a similar dietary supplement, comprising the bioactive ingredients of quail eggs and the zinc mineral, in the setting of active AR. Adult patients ($n = 77$), aged 18- 60 years, with mild, intermittent AR were enrolled in this single-arm, open-label trial. Patients' responses were assessed based on peak nasal inspiratory flow (PNIF) measurements at two visits (Day 1/Visit 1 and Day 7/Visit 2) and self-rating of AR-associated symptoms on a Visual Analog Scale (VAS) throughout the entire 7-day study period. PNIF values at 15, 30, 60, 90 and 120 min (Visit 1) following administration of an oral dose of the study product were the primary efficacy endpoint. PNIF values (Visit 1) gradually increased from baseline (pretreatment), with statistical significance first reached 30 min later ($p = 0.002$). VAS scores (Visit 1) for all AR symptoms gradually decreased with statistical significance first reached at 15 min (rhinorrhea, $p = 0.042$; itchy nose, $p = 0.001$; sneezing $p < 0.001$), 30 min (nasal congestion, $p < 0.001$; itchy eyes, $p = 0.003$) or 60 min (watery eyes, $p = 0.04$). PNIF improvement and decline of VAS scores were significantly more apparent at Visit one vs. Visit 2. Treatment-emergent adverse events were limited to cough and muscle strain (one patient each). Our results support the efficacy, rapid mode of action and tolerability of the investigated product for symptomatic treatment of mild intermittent AR.

KEYWORDS

allergic rhinitis; peak nasal inspiratory flow; quail eggs; visual analog scale

Introduction

Allergic rhinitis (AR) is the commonest atopic disease globally, affecting up to 30% of the adult population and 40% of children, with the highest rates reported in Western countries (Katelaris et al. 2012; Brożek et al. 2017). Given its frequent lack of

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recognition from patients and subsequent underdiagnosis (and undertreatment), these statistics are probably an underestimate of its true prevalence (Brożek et al. 2017; Gani et al. 2018). Most importantly, prevalence rates of AR have shown an alarming, almost two-fold increase as compared to those recorded approximately two decades ago, and are still on the rise, especially in previously low-prevalent countries (Schwindt and Settipane 2012; Brożek et al. 2017).

AR has been traditionally classified into two major subtypes, seasonal (SAR) and perennial (PAR), depending on the pattern and duration of symptoms (seasonal or year-round, respectively), with updated guidelines suggesting revision of its classification into "intermittent" and "persistent" groups (Brożek et al. 2017). AR symptoms mainly include episodic rhinorrhea, sneezing, nasal congestion and itching, with or without ocular involvement, following exposure to the culprit indoor or outdoor allergen(s), while their severity and functional impact among affected individuals vary considerably, ranging from mild to very severe (Brożek et al. 2017; Okubo, Gotoh et al. 2017; Okubo, Kurono et al. 2017). Despite lack of serious, life-threatening AR-associated morbidity, this chronic disease places a significant burden on society, in terms of quality-of-life (QoL) deterioration, use of healthcare resources and increase of direct (medical) and indirect costs (Zuberbier et al. 2014; Yoo et al. 2016; Brożek et al. 2017).

Intranasal corticosteroids are the cornerstone of AR pharmacotherapy, but their use is often hindered due to patients' fear of side effects, especially when long-term treatment for year-round symptoms is needed, stressing the need for treatments with improved tolerability (Hellings et al. 2012). A previous double-blind, placebo-controlled trial, evaluating the treatment effect and safety of a proprietary quail eggs-based blend (SniZtop®, Stragen SA, Switzerland) in subjects with induced symptoms of AR, showed efficient symptomatic relief and lack of adverse events (Benichou et al. 2014). We set out to investigate the efficacy and safety of a similar dietary supplement comprising the natural bioactive ingredients of SniZtop® and the zinc mineral, in adult patients with AR.

Methods

Subjects

Male or female patients, aged 18 to 60 years, with mild and intermittent AR symptoms at the time of pre-entry evaluation, not receiving any anti-allergic treatment for symptomatic control, and who were otherwise in good general health, were eligible for trial enrollment. Patients with severe and persistent rhinitis, requiring daily pharmacologic treatment, clinically significant comorbidities (i.e., cardiac or pulmonary disorders, known immunosuppression, e.t.c), known sensitivities to any of the ingredients of the study product, and pregnant or lactating women or patients who failed to provide written informed consent were excluded from the trial. Subjects suffering from asthma were included only if asthma symptoms were fully controlled within the last 6 months.

Study design

This study is a single-arm, open-label trial aiming to evaluate the efficacy of a commercially available dietary supplement in the form of chewable tablets comprising zinc and

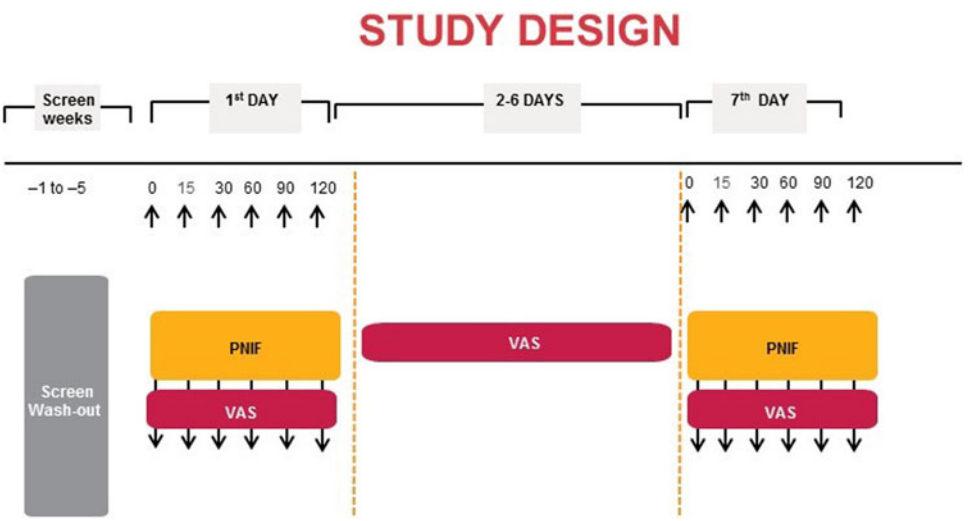

Figure 1. Study design.

the bioactive ingredients of SniZtop®, i.e., quail eggs blend and microcrystalline cellulose (LANES AlergEnd, Sarantis SA), as treatment of AR in adult patients. The trial protocol was approved by the local ethics commitees, and the study was conducted in accordance with the amended Declaration of Helsinki principles, and the Good Clinical Practice Guidelines. All study subjects provided written informed consent prior to their enrollment.

Patients were recruited by the investigators during standard care visits; those meeting all the inclusion criteria and none of the exclusion criteria were eligible for enrollment. At the screening/baseline visit (Visit 1), demographic and clinical data, including a detailed medical history, were obtained; a complete physical examination, recording of vital signs, and collection of urine samples from female subjects (so as to exclude pregnancy) were also carried out. The enrolled subjects were assigned a number to determine the sequence of study product administration. Patients were instructed to slowly chew two tablets of the study product as often as necessary, taking up to six tablets daily, throughout the trial duration (one week) and to write down on their calendars the amount of tablets they consumed per day and the time of day these were consumed. Visual analog scale (VAS) (range 0–100 mm; 0 = none, 100 = extreme symptoms) was used for self-rating of allergy symptoms (rhinorrhea, itchy nose, sneezing nasal congestion, itchy eyes and watery eyes) experienced by patients at the following time points: a) Visit 1: Time points = 0 min (before the oral consumption of the study product), and 15 min, 30 min, 60 min, 90 min, and 120 min (after its consumption), b) Visit 2 (+7 days from baseline): Time points = 0 min, 15 min, 30 min, 60 min, 90 min and 120 min and c) at night time during the 6 days period (day 1, 2, 3, 4, 5 and 6) and also at days 2, 3, 4, 5 and 6, 15 min after the consumption of the study product (Figure 1). VAS scales are highly sensitive and well validated tools for the subjective measurement of symptoms and quality of life evaluation in adults with AR, have been widely used in AR studies and have shown strong correlation with AR severity, both in trial and real-world settings (Demoly et al. 2013; Pfaar et al. 2014).

Peak nasal inspiratory flow (PNIF) average values were also measured at Visits 1 and 2 (at all time points from 0 to 120 min) for objective assessment of nasal patency. Three PNIF measurements were obtained at each time point for a more accurate evaluation of the average PNIF value.

Patients were allowed to use levocetirizine dihydrochloride 5 mg (once daily) as rescue medication during the first 4 days of the trial. A three-day wash out period (72 h) before visit two was mandatory. If any other rescue medication was used during the duration of the trial, these patients were considered as drop-outs. Additional rescue medication was also administered after the end of Visit 2, if necessary. Patients were monitored for adverse events by the investigator during the duration of the trial. Treatment-emergent adverse events were graded, according to their severity, as mild when they were perceived but easily tolerated by the patient, as moderate when they were cumbersome enough to impact daily activities, and as severe when they were life-threatening or considerably impairing daily activities.

Primary and secondary endpoints

The primary efficacy endpoint was the patient's response to the study product as measured by the average PNIF value at each time point of Visit 1. Secondary endpoints included safety and tolerability and additional efficacy evaluation of the study product, as measured by the average PNIF values at each time point of Visit 2, self-assessed VAS scores of nasal and ocular AR symptoms, and changes in the following efficacy variables: a) rate of change in the PNIF measurements between visit one and visit 2, b)all VAS scores at day 1 vs day 7, and c)night vs. morning variation of each nasal and ocular AR symptom.

Statistical analysis

Sample size

For this trial, the number of subjects recruited (77 patients) was adequate to show at least 5 units reduction in PNIF after 15 min, with 80% statistical power at 5% level of significance.

Analysis sets

Full Analysis Set (FAS): All enrolled subjects with at least one post-baseline efficacy assessment. The FAS was the primary analysis population and was used to assess the efficacy of the study product.

Per Protocol Population (PP): All enrolled subjects who completed the trial without major protocol deviations. Any analysis performed on the PP population was supportive to the primary analysis population.

Safety Evaluable Population (SEP): All enrolled subjects treated with the study drug. The safety analysis was based on the SEP.

Data analysis

Continuous data were summarized by the number of subjects (N), the arithmetic mean, the standard deviation, the coefficient of variation as a percentage (CV%), the median, the

minimum and the maximum value. Categorical data were summarized by absolute (N) and relative (%) frequency tables. PNIF and VAS scores were analyzed using analysis of variance for repeated measures. Efficacy and safety analysis was based on the FAS ($N = 77$) and SEP ($N = 77$) populations, respectively. Primary efficacy endpoint was also analyzed in the PP. Summary statistics of baseline characteristics are based on mean, standard deviation, median and range of values. All efficacy variables but PNIF were transformed to logarithmic scale prior to any statistical inference due to great variability of the values. Summary statistics are based on both observed data and Mixed Models analysis of Repeated Measures (MMRM) estimates. Summaries based on VAS scores are provided in back transformed values reported as geometric means followed by the corresponding 95% confidence intervals (CI); MMRM estimates are preferable for subjects' description since they are adjusted for other subject characteristics (e.g., age, sex etc).

The effect of the study product on PNIF site visit 1, was investigated by MMRM. The unstructured covariance matrix was used. Age was included in the model as covariate, time and sex were treated as fixed factors. The baseline PNIF values were not considered in the model due to convergence issues. Comparison from MMRM estimates at each time point with baseline were subject to Bonferroni adjustment of the corresponding p-value. MMRM estimates were summarized. The same analysis was considered for the assessment of all VAS scales at day 1.

The effect of the study product on PNIF site visit two over visit one to assess the rate of change over time, was investigated by MMRM as well. Modeling considered a random intercept assuming that the intercepts randomly distributed from a normal distribution. Age, cumulative number of tablets as well as the baseline PNIF values were included in the model as covariates, with time and sex treated as fixed factors. The rate of change in the PNIF measurements between visit one and visit two was assessed by the cross product of time and day (day*time) which was treated as fixed factor. The same analysis was considered for the assessment of all VAS scales at day 1 vs day 7.

The night vs. morning variation of each nasal and ocular symptom was assessed cumulatively between subjects who received extra tablets during the day and those who did not. All night measurements were compared to all morning measurements using a separate MMRM methodology accounting for the within patient variation and using an unstructured covariance matrix. Age, sex, day, time as well as the baseline symptom values were included in the model as covariates. MMRM estimates were summarized.

No imputation of missing data was performed since there were no eligible observations (one patient discontinued treatment at day 3; therefore there was not value to apply the last observation carried forward technique at day 7). All tests were 2-sided and level of significance was set at $\alpha = 0.05$.

Results

Demographics and clinical features of patients, treatment and follow-up data

Demographics and baseline clinical characteristics of patients are summarized in Table 1. After the initial screening, 77 subjects (male to female ratio: 44/33) were

Table 1. Baseline demographics and clinical features of patients (Full Analysis Set/FAS).

	N (%) 77(100%)	Mean	Standard Deviation	Minimum	Maximum
Age (years)		41.42	12.024	18	63
Sex					
Male	44 (57.1%)				
Female	33 (42.9%)				
Systolic blood pressure (mmHg)		121.62	12.709	85	150
Diastolic blood pressure (mmHg)		75.61	8.490	55	102
Weight (kgs)		75.86	14.833	43	125
Height (cm)		171.90	7.804	155	188
BMI (k/m^2)		25.52	3.809	18	41
Breath rate (br/min)		14.76	2.129	10	18
Comorbidities					
Yes	30 (38.96%)				
No	44 (57.14%)				
Type of comorbidities					
Asthma	15 (19.48%)				
Hypersensitivity/Allergic disorders	5 (5.17%)				
Endocrine disorders	3 (3.9%)				
Gastrointestinal disorders	2 (2.6%)				
Vascular disorders	2 (2.6%)				
Skin/subcutaneous disorders	2 (2.6%)				
Metabolism/nutrition disorders	1 (1.3%)				

enrolled and comprised the FAS population. Mean age (± SD) was 41.42 (±12.02) years. The commonest comorbidity among enrolled subjects was asthma, reported in 15/77 patients (19.48%), followed by hypersensitivity/allergic disorders (5/77, 5.17%), endocrine disorders (3/77, 3.9%), gastrointestinal, vascular and skin/subcutaneous disorders (2/77 each, 2.60%) and metabolism/nutrition disorders (1/77, 1.30%).

The study protocol was completed without any violations by 76/77 enrolled subjects (98.7%) (PP population). One subject withdrew from the trial due to occurrence of an adverse event (cough) at day 3 of the trial period. The mean number (± SD) of the study product (tablets) received was 14.6 ± 4.78 tablets (range 8–44) with a median of 12 tablets. The percentage of subjects who received extra tablets (of the study product) at night ranged from 2.6% (day 1) to 18.4% (day 3).

Efficacy and safety evaluations

PNIF measurements

Mean PNIF values, based on observed data, at each time point of visits 1 and 2, are presented in Table 2. PNIF values at each time point of visit 1, based on MMRM models adjusted for sex and age, for the FAS and PP populations, are depicted in Table 3. PNIF value (FAS) gradually increased from baseline (day 1/time point = 0), following oral consumption of the study product, with statistical significance first reached at the time point = 30 min, after its increase by 3.2 units ($p = 0.002$) (Table 3, Figure 2). Results were similar in the PP population. When the rate of PNIF improvement over the 120 mins was compared between the two visits (day 1 and day 7), based on MMRM models adjusted for sex, age, total number of tablets received and baseline PNIF, increase was significantly more apparent at Visit 1 ($p < 0.001$) (Figure 2).

Table 2. Peak nasal inspiratory flow (PNIF) values, based on observed data, at each visit (Full Analysis Set/FAS).

Day/visit	Time (min)	N	Mean	Standard Deviation	Median	Minimum	Maximum
D1 /Visit 1	0	77	83.010	32.6862	70.000	41.7	153.3
	15	77	84.479	33.5896	68.300	45.0	175.0
	30	77	86.209	33.2243	68.300	45.0	163.3
	60	77	89.283	34.0040	76.700	33.3	196.7
	90	77	92.988	32.9394	78.300	50.0	193.3
	120	77	94.764	32.8539	80.000	46.7	185.0
D7/Visit 2	0	76	96.951	30.7246	85.850	41.7	190.0
	15	76	100.374	30.2575	90.000	55.0	188.3
	30	76	101.642	30.8889	90.000	53.3	193.3
	60	76	102.784	32.3586	91.700	46.7	220.0
	90	76	103.932	32.8595	91.700	55.0	225.0
	120	76	105.130	32.7398	92.500	53.3	216.7

Table 3. Peak nasal inspiratory flow (PNIF) values, based on MMRM estimates, at visit 1 (Full Analysis Set/FAS and Per Protocol Population/PP).

Day 1/Time (min)	Mean	95% Confidence Interval		P (t = 0 vs*)
Full Analysis Set/FAS				
0	81.801	74.456	89.147	
15	83.270	75.750	90.791	0.437
30	85.000	77.582	92.418	0.002
60	88.074	80.468	95.680	<0.001
90	91.779	84.432	99.127	<0.001
120	93.555	86.215	100.894	<0.001
Day 1/Time (min)	Mean	95% Confidence Interval		P (t = 0 vs*)
Per Protocol Population/PP				
0	82.163	74.775	89.550	
15	83.607	76.039	91.176	1
30	85.315	77.847	92.784	0.008
60	87.903	80.209	95.598	0.001
90	91.768	84.336	99.200	<0.001
120	93.501	86.076	100.925	<0.001

VAS measurements

VAS scores were significantly improved for all allergy symptoms following administration of the study product. VAS scores at each time point of visit 1, based on MMRM models adjusted for sex and age, for the FAS population, are depicted in Tables 4 and 5. VAS scores for rhinorrhea, itchy nose, and sneezing, gradually decreased from baseline (day 1/time point = 0), following oral consumption of the study product, with statistical significance first reached at the time point = 15 min, after their decrease by 4.464 units ($p = 0.042$), 5.699 units ($p = 0.001$) and 10.736 units ($p < 0.001$), respectively (Table 4, Figure 3). When the rate of decline in VAS scores for each of the above symptoms was compared between the two visits (day 1 and day 7), based on MMRM estimates adjusted for sex, age, total number of tablets received and baseline VAS scores, decrease was significantly more apparent at day 1 ($p = 0.025$, $p < 0.001$ and $p < 0.001$, respectively) (Figure 3).

VAS scores for nasal congestion and itchy eyes gradually decreased from baseline as well, with statistical significance first reached at the time point = 30 min, after their decrease by 6.569 units ($p < 0.001$) and 2.583 units ($p = 0.003$), respectively (Table 5). When the rate of decline in VAS scores was compared between the two visits (day 1

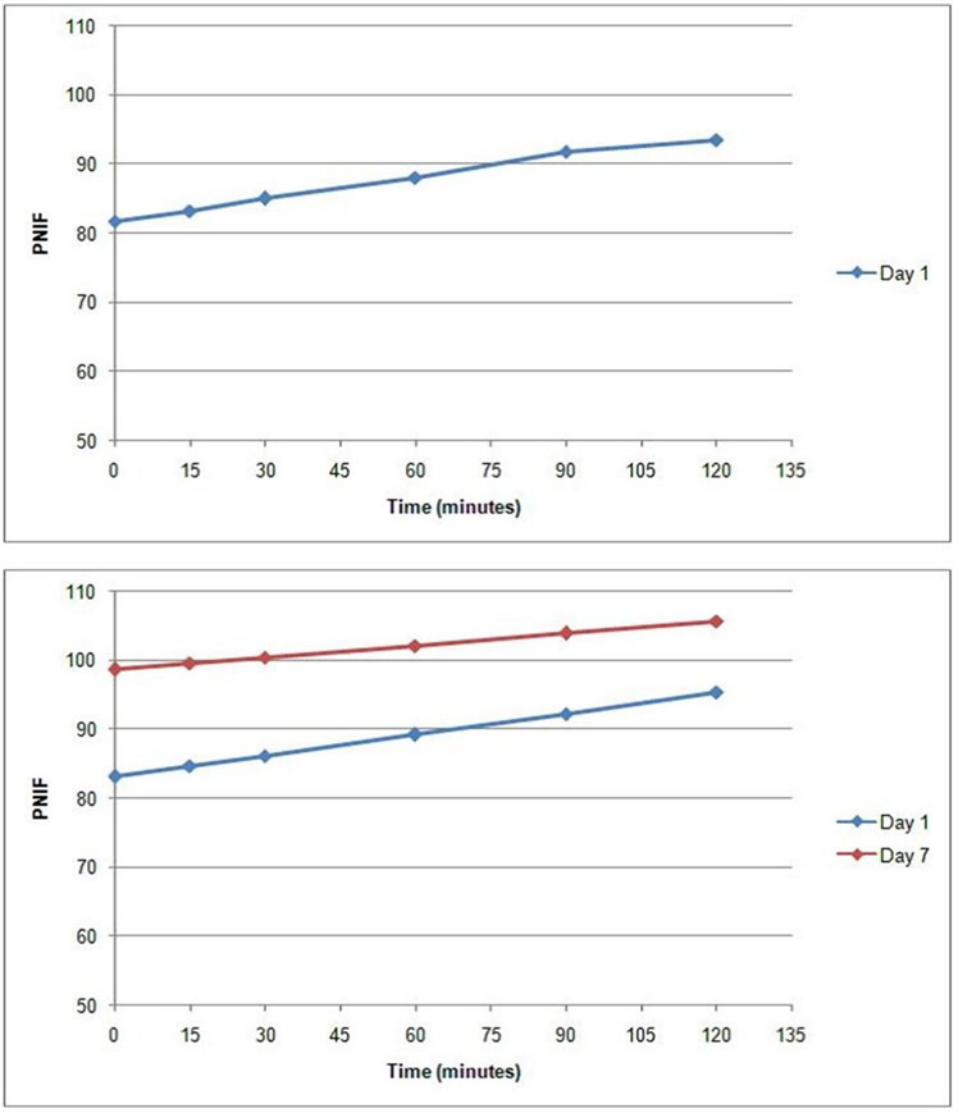

Figure 2. Peak nasal inspiratory flow (PNIF) values (day 1, all time points), based on MMRM estimates and rate of PNIF improvement over the 120 min at each separate visit (Visit 1/Day 1 and Visit 2/Day 7) ($p < 0.001$) (Full Analysis Set/FAS).

and day 7), based on MMRM estimates adjusted for sex, age, total number of tablets received and baseline VAS scores, no statistically significant difference was observed for nasal congestion ($p = 0.078$), while decrease for itchy eyes was significantly more apparent at day 1 ($p = 0.001$).

VAS scores for watery eyes gradually decreased from baseline, with statistical significance first reached at the time point = 60 min, after their decrease by 1.861 units ($p = 0.040$) (Table 5). When the rate of decline in VAS scores was compared between the two visits (day 1 and day 7), based on MMRM estimates adjusted for sex, age, total

Table 4. Visual analog scale (VAS) scores for rhinorrhea, itchy nose and sneezing, based on MMRM estimates, at visit 1 (Full Analysis Set/FAS).

Day 1/Time (min)	Geometric Mean	95% Confidence Interval		P (t = 0 vs*)
Rhinorrhea				
0	18.629	14.019	24.647	
15	14.165	10.407	19.165	0.042
30	10.623	7.511	14.880	0.001
60	10.112	7.230	14.006	0.001
90	8.574	5.985	12.129	<0.0001
120	6.933	4.754	9.931	<0.0001
Day 1/Time (min)	Geometric Mean	95% Confidence Interval		P (t = 0 vs*)
Itchy nose				
0	15.979	11.510	22.035	
15	10.280	7.124	14.671	0.001
30	7.012	4.692	10.276	<0.001
60	5.547	3.609	8.299	<0.001
90	4.291	2.747	6.474	<0.001
120	3.389	2.127	5.156	<0.001
Day 1/Time (min)	Geometric Mean	95% Confidence Interval		P (t = 0 vs*)
Sneezing				
0	20.563	15.395	27.338	
15	9.827	6.707	14.213	<0.001
30	7.525	5.088	10.933	<0.001
60	5.527	3.588	8.283	<0.001
90	5.284	3.445	7.887	<0.001
120	3.112	1.917	4.803	<0.001

Table 5. Visual analog scale (VAS) scores for nasal congestion, itchy eyes and watery eyes, based on MMRM estimates, at visit 1 (Full Analysis Set/FAS).

Day 1/Time (min)	Geometric Mean	95% Confidence Interval		P (t = 0 vs*)
Nasal congestion				
0	32.182	32.187	32.190	
15	30.976	27.798	34.502	1
30	25.523	23.116	28.143	<0.001
60	21.851	18.308	26.049	<0.001
90	17.560	14.300	21.527	<0.001
120	15.428	11.768	20.119	<0.001
Day 1/Time (min)	Geometric Mean	95% Confidence Interval		P (t = 0 vs*)
Itchy eyes				
0	6.114	3.904	9.319	
15	4.534	2.877	6.893	0.083
30	3.531	2.200	5.417	0.003
60	2.651	1.586	4.155	<0.001
90	2.536	1.563	3.884	<0.001
120	1.798	1.024	2.865	<0.001
Day 1/Time (min)	Geometric Mean	95% Confidence Interval		P (t = 0 vs*)
Watery eyes				
0	4.089	2.512	6.375	
15	3.208	1.940	5.019	0.848
30	2.762	1.680	4.284	0.379
60	2.228	1.305	3.523	0.040
90	1.614	0.906	2.585	0.001
120	1.421	0.765	2.316	<0.001

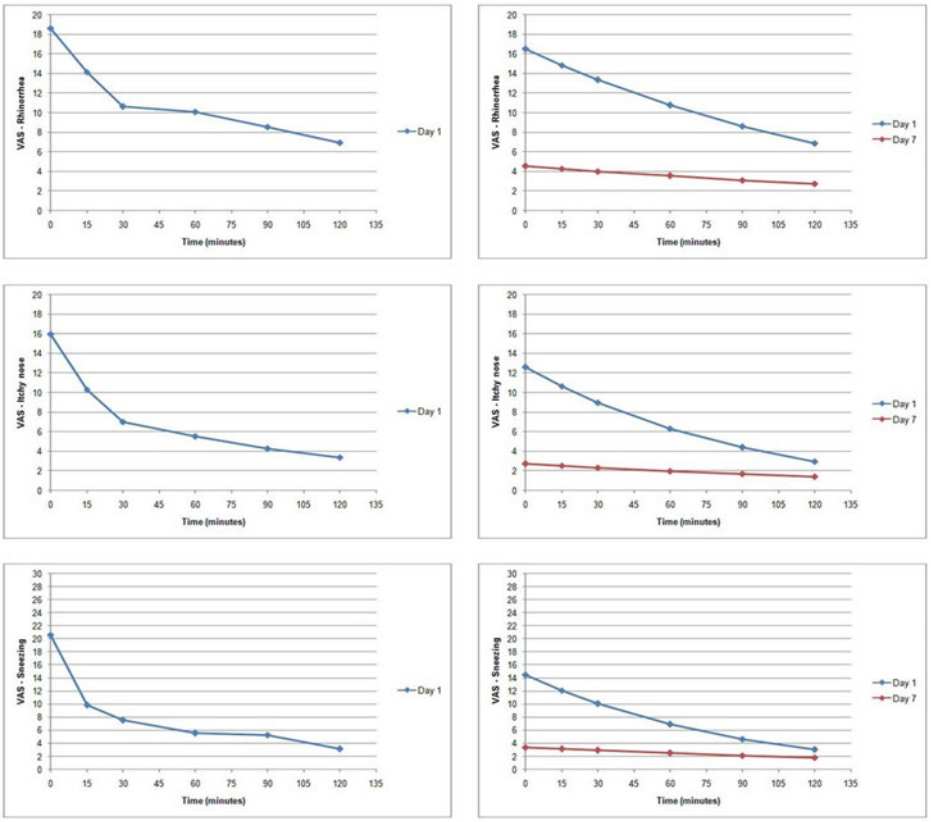

Figure 3. Visual analog scale (VAS) scores for rhinorrhea, itchy nose and sneezing (day 1, all time points), based on MMRM estimates and rate of VAS scores decline for the above symptoms over the 120 min at each separate visit (Visit 1/Day 1 and Visit 2/Day 7) ($p = 0.025$, $p < 0.001$ and $p < 0.001$, respectively) (Full Analysis Set/FAS).

number of tablets received and baseline VAS scores, decrease was significantly more apparent at day 1 ($p = 0.001$).

Night versus morning variation of VAS scores for itchy nose was significantly higher in subjects who took extra tablets during the day as compared to those who were receiving only the morning tablets ($p = 0.022$); however, no statistically significant difference was observed for rhinorrhea ($p = 0.493$), sneezing ($p = 0.466$), nasal congestion ($p = 0.093$), itchy eyes ($p = 0.342$) or watery eyes ($p = 0.342$).

Adverse events were reported in 2 subjects (muscle strain and cough, respectively; the second subject withdrew from the study). Finally, neither levocetirizine nor any other rescue medication was used by any of our patients for symptoms control.

Discussion

In the current clinical trial, the study product (a dietary supplement comprising the bioactive natural ingredients of quail eggs blend and zinc) resulted in improvement of nasal flow and patency in adult patients with active symptoms of mild/intermittent AR, as documented by the statistically significant increase of PNIF, after product

administration, in comparison to baseline (pretreatment) values. A statistically significant decline of VAS scores for all AR-associated symptoms was also observed, which was more pronounced for nasal (rhinorrhea, sneezing, itchy nose) as compared to ocular symptoms (itchy and watery eyes). Notably, both PNIF and VAS improvements reached statistical significance within 15–30 min from product administration, with the exception of one type of ocular symptoms (watery eyes) which took longer to respond (60 min). These data indicate a significant symptomatic effect of the investigated product, in terms of both objective and subjective measures, and a rapid mode of action. Excellent safety and tolerability was also documented, since treatment-emergent adverse events were rare (2/77 patients) and mild (cough and muscle strain in one patient each), leading to discontinuation of treatment in one patient only.

In line with our present findings, a previous randomized, double-blind, placebo-controlled trial supported the efficacy and safety of a proprietary quail eggs blend (SniZtop®) for symptomatic treatment of AR symptoms (Benichou et al. 2014). Following a nasal allergy challenge, for exposure of predisposed subjects to a combination of aerosolized antigens and induction or AR symptoms, an acute oral dose of the study product was administered. As shown by comparative analysis of PNIF measurements and patient-assessed VAS scores as well as total IgE determination (before and after SniZtop® intake), the study product resulted in significant relief of AR symptoms, without emergence of any treatment-related adverse events (Benichou et al. 2014). More specifically, with regard to PNIF values, the study product resulted in significantly improved nasal patency and breathing as compared to placebo, with statistical significance first reached at 15 min post administration, exactly as observed in the current trial. Furthermore, also in accordance with the present study, VAS scores for nasal obstruction, rhinorrhea, watery eyes, itchy eyes, and itchy nose, reflecting the subjective effect of AR symptoms on the well-being of patients, as perceived and assessed by the patients themselves, were significantly decreased in the active treatment arm. Sneezing was the only symptom not significantly affected by the active product, in contrast with the respective results of our trial which revealed a significant improvement of sneezing-related VAS scores following product administration. Given the lack of any statistically significant IgE modifications after product intake, the authors of the previous trial hypothesized that the mechanism of action of its active ingredients may be IgE-independent (Benichou et al. 2014).

As previously described, quail eggs are composed of water (68%), proteins, mainly ovomucoids (12%), fats (10%), minerals (8%) and carbohydrates (2%) (Prelipcean (Teuşan) et al. 2012), while *in vitro* data have shown that ovomucoids in particular may act as inhibitors of serine proteases (Feeney et al. 1969; Takahashi et al. 1994; Vergnaud and Bruttmann 2007). These enzymes have the propensity to elicit tissue injury and induce IgE-mediated allergic response, hence, inhibition of serine proteases by quail eggs ovomucoids may, theoretically, result in inhibition of the cascade of immune-related allergic responses and attenuation of the allergic reaction (Widmer et al. 2000; Benichou et al. 2014). Interestingly, a recent preclinical study showed that oral quail egg treatment was effective in attenuating immune responses and alleviating symptoms in peanut-sensitized mice with eosinophilic esophagitis-like disease induced by food allergy, further supporting the potent anti-allergic effects of this supplement (Lianto et al. 2018).

Zinc is an essential mineral, with various beneficial properties and a well-established effect on a large variety of vital physiological processes, mediated through its numerous immunoregulatory, anti-inflammatory and antioxidant functions (Zalewski et al. 2005). A proposed, but yet unconfirmed, anti-inflammatory mechanism of zinc involves blocking of the interaction between a cell surface antigen of neutrophils, leucocyte-associated antigen 1, and intracellular adhesion molecule 1 (ICAM-1), another cell surface antigen which is expressed not only by inflammatory cells but epithelial cells as well, including the nasal epithelium, and mediates the inflammatory response in AR (Novick et al. 1997; Demoly et al. 1998; Zalewski et al. 2005). Oral zinc supplementation has also been shown to suppress inflammation of the airway epithelium in animal models (Lu et al. 2012), to improve lung function in patients with cystic fibrosis (Demoly et al. 1998), to benefit patients with atopic asthma, common cold, lower respiratory tract infections, pneumonia and tuberculosis and to decrease incidence of respiratory tract infections in children (Van Biervliet et al. 2008; Prasad 2009; Mohamed et al. 2018) but its potential clinical benefit in AR remains to be established.

Use of a natural product, essentially free of side effects and with minimal contraindications, such as the dietary supplement herein investigated, is, undoubtedly, an appealing option for symptomatic treatment of AR. The existing data are, nevertheless, too limited to draw any solid conclusions, while the efficacy of this product in comparison to that of standard antiallergic pharmacotherapies, its long-term efficacy and safety, its effect on more severe forms of AR and its potential use as an add-on to existing treatments, are all important issues which remain to be explored. With regard to current trial results in particular, adequate emphasis must be placed on some inherent limitations of our study design, mainly including the absence of a placebo-controlled arm, the open-label design and lack of laboratory investigations for the assessment of the potential mechanism of action of the study product.

In conclusion, the results of this trial suggest that the natural product investigated may be safe and effective for symptomatic treatment of mild AR. Given our study limitations (single-arm, open label design), these data warrant confirmation in future randomized placebo-controlled trials. Head-to-head trials, comparing this product with available standard-of-care treatments are also needed so as to delineate more clearly its exact therapeutic value and overall clinical significance.

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